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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/940,550	08/27/2001	Luke Mankin	16313-0055	4978

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EXAMINER
FOX, DAVID T

ART UNIT	PAPER NUMBER
1638	14

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/940,550	Mankin et al
Examiner	**Group Art Unit**
FOX	1638

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE -3- MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

- [x] Responsive to communication(s) filed on 3/17/03.
- [ ] This action is **FINAL.**
- [ ] Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

- [x] Claim(s) 1-60 is/are pending in the application.
  - Of the above claim(s) 10-20, 26, 28, 29, 39-60 is/are withdrawn from consideration.
- [ ] Claim(s) _____ is/are allowed.
- [x] Claim(s) 1-9, 21-25, 27, 30-38 is/are rejected.
- [ ] Claim(s) _____ is/are objected to.
- [ ] Claim(s) _____ are subject to restriction or election requirement.

Application Papers

- [ ] See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- [ ] The proposed drawing correction, filed on _____ is [ ] approved [ ] disapproved.
- [ ] The drawing(s) filed on _____ is/are objected to by the Examiner.
- [ ] The specification is objected to by the Examiner.
- [ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

- [ ] Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).
  - [ ] All [ ] Some* [ ] None of the CERTIFIED copies of the priority documents have been
  - [ ] received.
  - [ ] received in Application No. (Series Code/Serial Number) _____.
  - [ ] received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

- [x] Information Disclosure Statement(s), PTO-1449, Paper No(s). 3 + 11
- [ ] Interview Summary, PTO-413
- [x] Notice of Reference(s) Cited, PTO-892
- [ ] Notice of Informal Patent Application, PTO-152
- [ ] Notice of Draftsperson's Patent Drawing Review, PTO-948
- [ ] Other _____

Office Action Summary

Applicant's election with traverse of Group I in Paper No.13 is acknowledged. The traversal is on the ground(s) that there would be no burden to search all of the inventions of Groups I-V, that an election of species would have been more appropriate, and that up to five species are generally permitted. This is not found persuasive because each invention requires not only a different promoter, but also different means for inducing or activating the expression of the recombinase gene, each of which would require a separate search. The method of generating seedless plants or aborted-germinating seeds of Group II requires the search for genes encoding toxic products as well as methods for evaluating seedlessness or aborted germination, each not required by any other group. In addition, the method for controlling hybridization via the generation of male- sterile plants (Group III) also requires the search for genes encoding toxic peptides as well as methods of crop hybridization, each not required by the other groups. The method of Group IV requires methods for determining disease susceptibility of each host plant, in order to obtain pathogen-inducible recombinase gene expression, not required by any other group. The method of Group V requires methods and compositions for seed coating, not required by any other group.

Since the inventions of Groups I-V are not merely variants of each other, but in fact constitute different inventive concepts, election of species is not applicable. Furthermore, within the single elected Group, namely developmentally-regulated promoters, the Examiner has permitted the examination of several species, including leaf-, root-, meristem- and tuber- preferred promoters.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-9, 21-25, 27 and 30-38 are examined to the extent that they read on the elected invention. Claims 1, 8-9, 30 and 37-38 are objected to for encompassing non-elected subject matter, namely "regulatable" promoters other than somatic tissue-preferred promoters. Claims 21-25 are objected to for depending upon non-elected claims.

Claims 21-25 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim can only depend upon another multiply dependent claim in the alternative. See MPEP § 608.01(n). In the interest of compact prosecution, the claims have been treated on the merits. Such treatment does not relieve Applicants of the responsibility to respond to this objection.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9, 21-25, 27 and 30-38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to polynucleotides comprising a multitude of somatic tissue-preferred promoters, including leaf-, root-, meristem- and tuber- preferred promoters, from a multitude of plant and gene sources and of a multitude of sequences; methods for their use; and

plant cells and plants transformed therewith. In contrast, the specification provides no guidance for the characterization or description of any somatic tissue-preferred promoter in terms of sequence or gene source, and no plant cell or plant transformed with any of said promoters was reduced to practice.

The Federal Circuit has recently clarified the application of the written description requirement. The court stated that a written description of an invention "requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials." *University of California* v. *Eli Lilly and Co.*, 119 F.3d 1559, 1568; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The court also concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." *Id.* Further, the court held that to adequately describe a claimed genus, Patent Owner must describe a representative number of the species of the claimed genus, and that one of skill in the art should be able to "visualize or recognize the identity of the members of the genus." *Id.*

See MPEP Section 2163, page 156 of Chapter 2100 of the August 2001 version, column 2, bottom paragraph, where it is taught that

> [T]he claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence.

Given the claim breadth and lack of guidance as discussed above, the specification fails to provide an adequate written description of the genus of sequences as broadly claimed. Given the lack of written description of the claimed genus of sequences, any method of using them, such as transforming plant cells and plants therewith, and the resultant products including the claimed transformed plant cells and plants containing the genus of sequences, would also be inadequately described. Accordingly, one skilled in the art would not have recognized Applicant to have been in possession of the claimed invention at the time of filing. See the Written Description Requirement guidelines published in Federal Register/ Vol. 66, No. 4/ Friday January 5, 2001/ Notices: pp. 1099-1111).

See also Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ 2d 1016 at 1021, (Fed. Cir. 1991) where it is taught that a gene (which includes a promoter) is not reduced to practice until the inventor can define it by "its physical or chemical properties" (e.g. a DNA sequence).

See also *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), which teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism.

Claims 1-9, 21-25, 27, and 30-38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims limited to polynucleotides comprising a plant somatic tissue-specific promoter ligated to a gene encoding a theta C31 recombinase for the

controlled excision of desired trait polynucleotides in plants, wherein the polynucleotides are flanked by recombination sites which are recognized by the theta C31 recombinase, does not reasonably provide enablement for claims broadly drawn to any somatic tissue-specific promoter functional in non-plant organisms such as animals, or any other recombinase-encoding gene, or the use of the theta C31 recombinase with non-corresponding recombination recognition sites such as loxP or FRT. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1-2, 6-9, 21-25, 27, 30-31 and 35-38 are broadly drawn to polynucleotides encoding a multitude of recombinases from a multitude of sources, including reversible and irreversible recombinases, and their use to effect controlled excision of transgenes. Claims 1-6, 8, 21-25, 27, 30-35 and 37 are broadly drawn to polynucleotides comprising any developmentally regulatable promoter functional in any organism including animals. All the claims are broadly drawn to any of a multitude of recombination sites. No guidance is provided for polynucleotides comprising any animal-functional promoters or methods of animal transformation, and no guidance is provided for polynucleotides comprising any other type of recombinase gene other than the theta C31 recombinase gene for controlled and permanent transgene excision in transformed plants. In addition, no guidance is provided for successful recombinase-mediated excision when non-corresponding recombination recognition sites are used.

Recombinase-mediated transgene deletion is unpredictable. As admitted by Applicants on page 10 of the specification, paragraph 31 through page 11 of the specification, paragraph 32, irreversible recombinases are preferred because the transgene deletion is stable, since no recombination between recombinase-recognition sites occurs. See also Vergunst et al, page 2732, top paragraph of each column, and page 2733, top paragraph of column 2; who teach that Cre recombinase-mediated transgene manipulation is hampered by instability and rearragements.

Furthermore, it is well-known in the art that tissue-specific and developmentally regulated promoters will not function in divergent tissues, since the chemical stimuli required for their activation is not present. Thus, animal-derived tissue-specific or developmentally regulated promoters will not function in transformed plant tissue.

Given the claim breadth, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to identify a multitude of recombinase genes from a multitude of sources, to isolate the corresponding genes encoding them, and to evaluate the ability of these recombinase genes to effect stable and permanent deletion of unwanted transgenes. Undue experimentation would have also been required to identify and isolate a multitude of animal-derived developmentally regulated genes and their corresponding promoters, and to obtain successful function of animal-derived developmentally regulated promoters in plant tissue. Finally, undue experimentation would have been required to obtain successful transgene excision via the use of a particular recombinase and non-corresponding recombination sites.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 6-9, 21-23, 30-31 and 35-38 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 97/37012 (COMMONWEALTH).

The claims are broadly drawn to polynucleotides comprising any desired trait polynucleotide including a selectable marker and a recombinase-encoding polynucleotide including Cre, both operably linked to a developmentally regulatable promoter including a leaf-preferred promoter, all flanked by a pair of directly oriented recombination sites including loxP; methods for their use to transform plants and cause excision of unwanted trangenes; and the resultant dicotyledonous transformed plant cells and plants.

COMMONWEALTH teach polynucleotides comprising a selectable marker or a morphology-altering/regeneration-enhancing "desired trait polynucleotide" and a Cre recombinase polynucleotide, operably linked to the leaf-specific rbcS (RUBISCO) promoter, all flanked by directly oriented loxP recombination sites; for the excision of unwanted transgenes which either pose an environmental or health threat, or which cause an unwanted metabolic or genetic load, after their initial expression in particular cell types; and transformed tobacco cells and plants (see, e.g., page 2, lines 8-24; page 4, line 26 through page 5, line 19; page 10, lines 25-29; page 11,

lines 16-21 and 27-28; page 13, lines 6-24; pages 14-15; page 16, line 27 through page 17, line 4; page 17, line 25 through page 18, line 3; page 18, line 14 through page 19, line 21; page 21, lines 3-11; page 37, line 18 through page 38; page 42; page 45, line 15 through page 46; page 48, line 10 through page 49, line 21; page 50, lines 10-19).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2, 6-9, 21-22, 24-25, 30-31 and 35-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 97/37012 (COMMONWEALTH) taken with Arntzen et al (U.S. 5,792,935).

The claims are broadly drawn to transformed monocots containing an excisable polynucleotide comprising a recombinase gene, a trait gene of interest, and optionally an additional selectable marker gene; operably linked to a developmentally regulated promoter; all flanked by directly oriented recombination sites.

COMMONWEALTH teach dicotyledonous plants transformed with such an excisable construct as discussed above, and also teach the advantages of incorporating multiple genes in a single construct (see, e.g., page 21, lines 3-11), and also suggest the transformation of monocotyledonous plants such as banana (see, e.g., page 5, lines 13-19).

COMMONWEALTH does not teach transformed banana plants.

Arntzen et al teach methods for transforming banana (see entire document).

It would have been obvious to one of ordinary skill in the art to utilize the excisable polynucleotide taught by COMMONWEALTH and to transform monocots such as banana with it, as suggested by COMMONWEALTH, using the methods of Arntzen et al. Choice of selectable marker gene or trait gene of interest would have been the optimization of process parameters.

Claims 1-2, 6-9, 21-22, 25, 27, 30-31 and 35-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 97/37012 (COMMONWEALTH) taken with Sederoff et al (U.S. 4,886,937).

The claims are broadly drawn to transformed trees containing an excisable polynucleotide comprising a recombinase gene, a trait gene of interest, and optionally an additional selectable

marker gene; operably linked to a developmentally regulated promoter; all flanked by directly oriented recombination sites.

COMMONWEALTH teach dicotyledonous plants transformed with such an excisable construct as discussed above, and also teach the advantages of incorporating multiple genes in a single construct (see, e.g., page 21, lines 3-11), and also suggest the transformation of trees such as pine (see, e.g., page 5, lines 13-19).

COMMONWEALTH does not teach transformed pine plants.

Sederoff et al teach methods for transforming pine (see entire document).

It would have been obvious to one of ordinary skill in the art to utilize the excisable polynucleotide taught by COMMONWEALTH and to transform trees such as pine with it, as suggested by COMMONWEALTH, using the methods of Sederoff et al. Choice of selectable marker gene or trait gene of interest would have been the optimization of process parameters.

Claims 3-5 and 32-34 are deemed free of the prior art, given the failure of the prior art to teach or reasonably suggest plant transformation with an excisable polynucleotide comprising the theta C31 recombinase gene in combination with a trait gene, operably linked to a developmentally regulatable promoter, all flanked by directly oriented recombination sites.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David T. Fox whose telephone number is (703) 308-0280. The examiner can normally be reached on Monday through Friday from 10:30AM to 7:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached on (703) 306-3218. The fax phone number for this Group is (703) 872-9306. The after final fax phone number is (703) 872-9307.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

June 2, 2003

DAVID T. FOX
PRIMARY EXAMINER
GROUP 1800 1638